THE FORMAMIDE$_2$-H_2O COMPLEX: STRUCTURE AND HYDROGEN BOND COOPERATIVE EFFECTS

SUSANA BLANCO

PABLO PINACHO

JUAN CARLOS LÓPEZ

Departamento de Química Física

Universidad de Valladolid, Valladolid

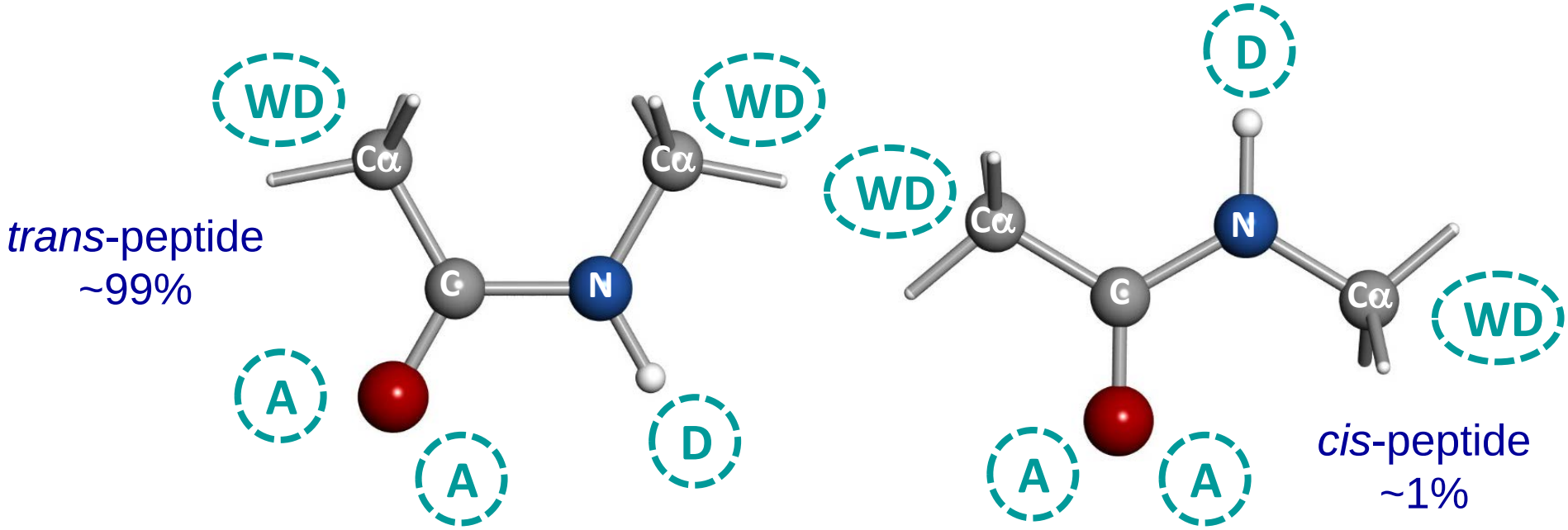
SPAIN

Introduction

Peptide groups in biomolecules may adopt ***cis*** or ***trans*** configurations

These present a variety of hydrogen bond interactions sites:

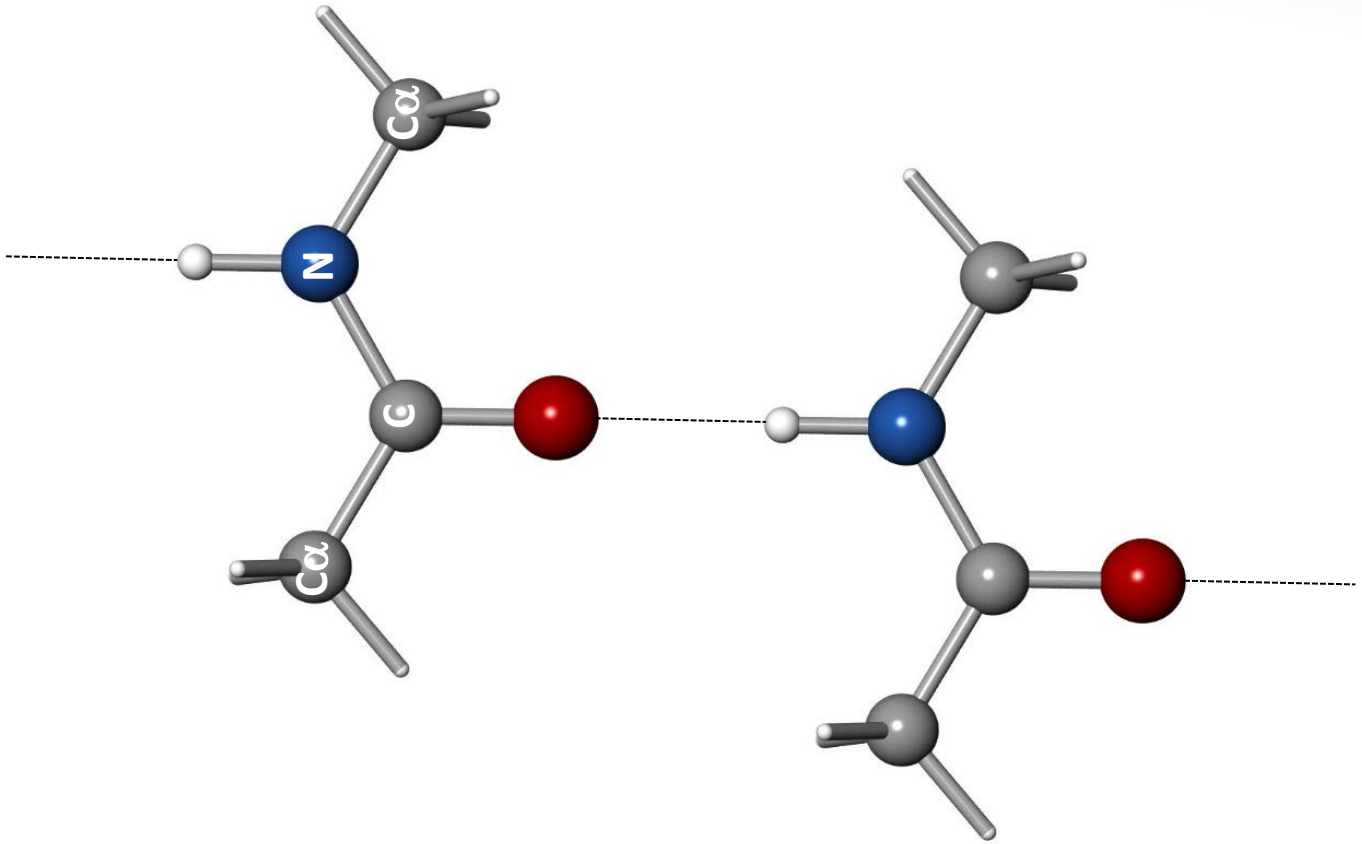
- proton acceptor (**A**)
- proton donor (**D**)
- weak hydrogen bonds (**WD**) (if including the C_α-H groups)



Introduction

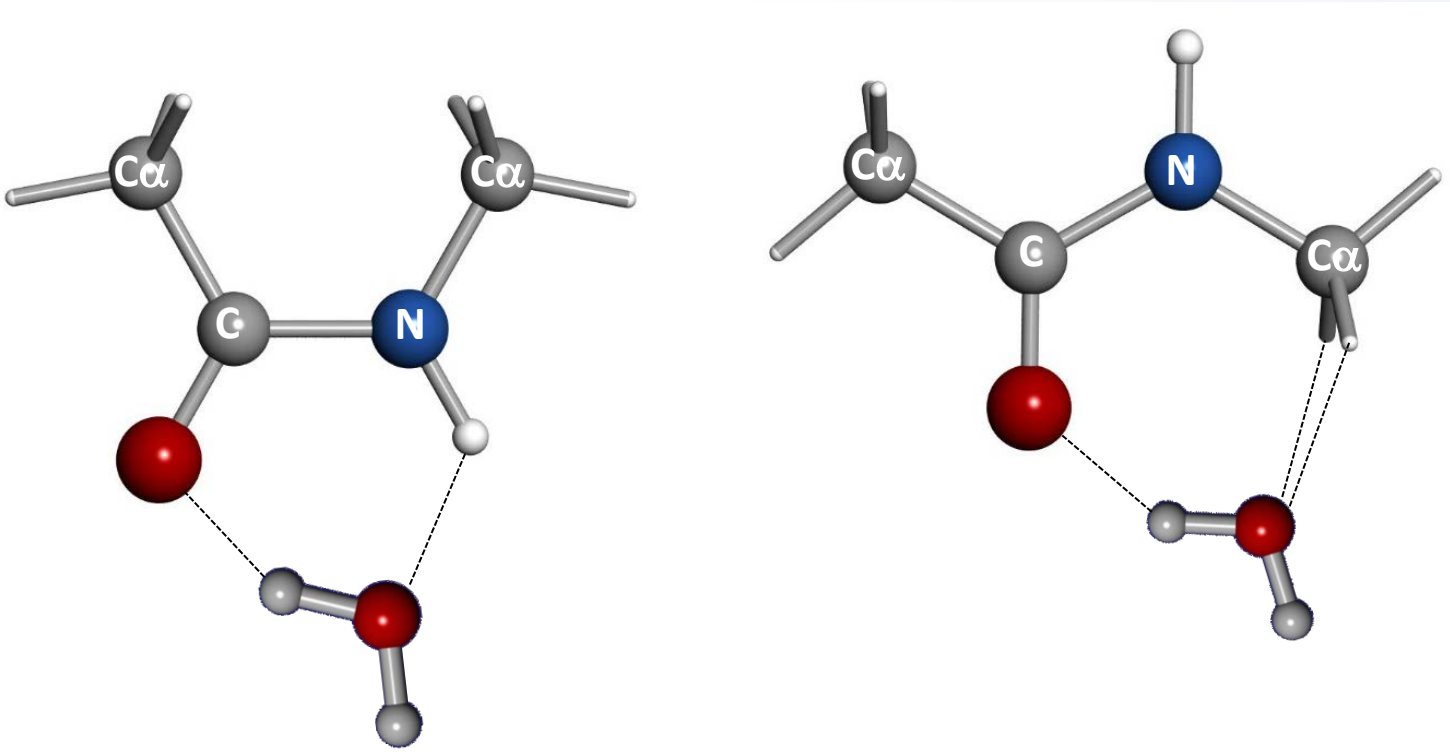
They made possible the interaction between peptide groups:

The C=O···H-N bond dominate in the hydrophobic core of proteins.



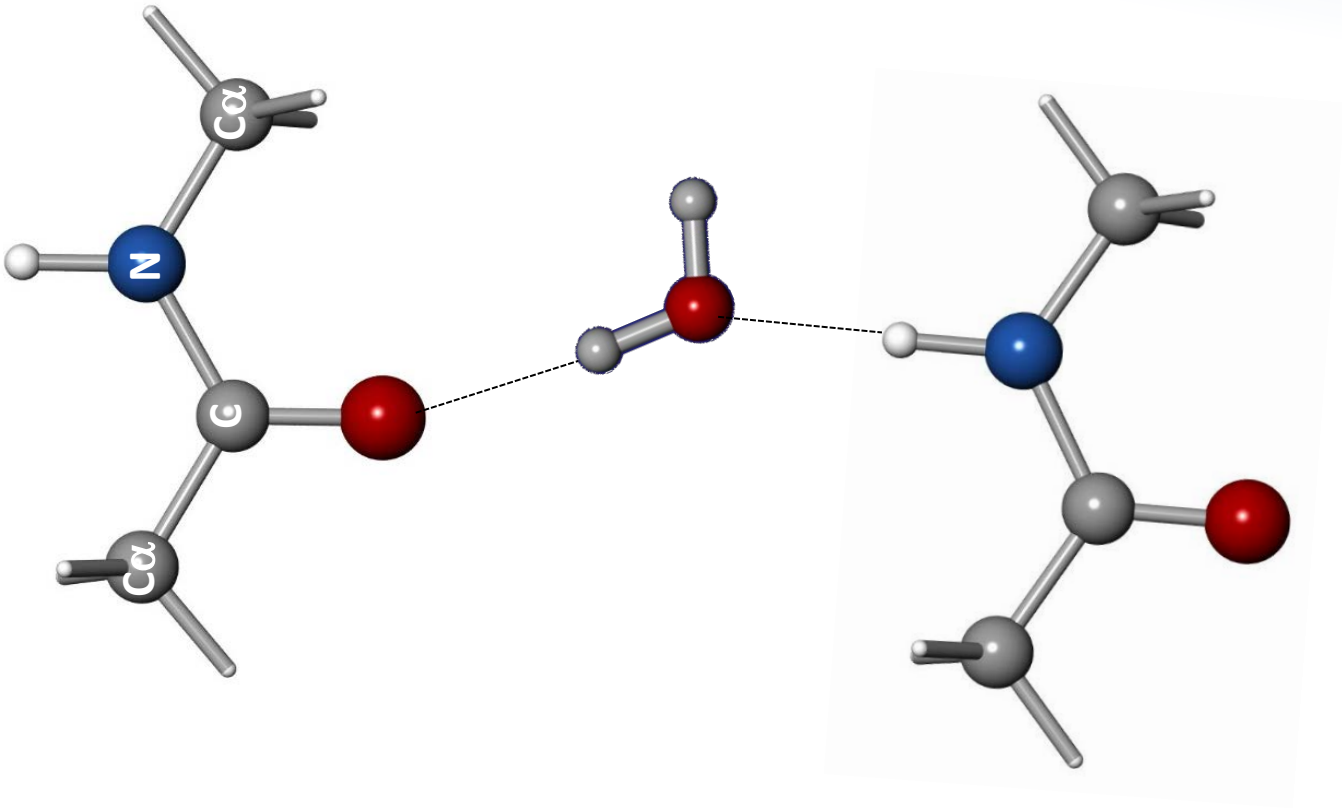
Introduction

These sites define a variety of possible interactions of peptide group with water: C=O···HOH: ~44 %



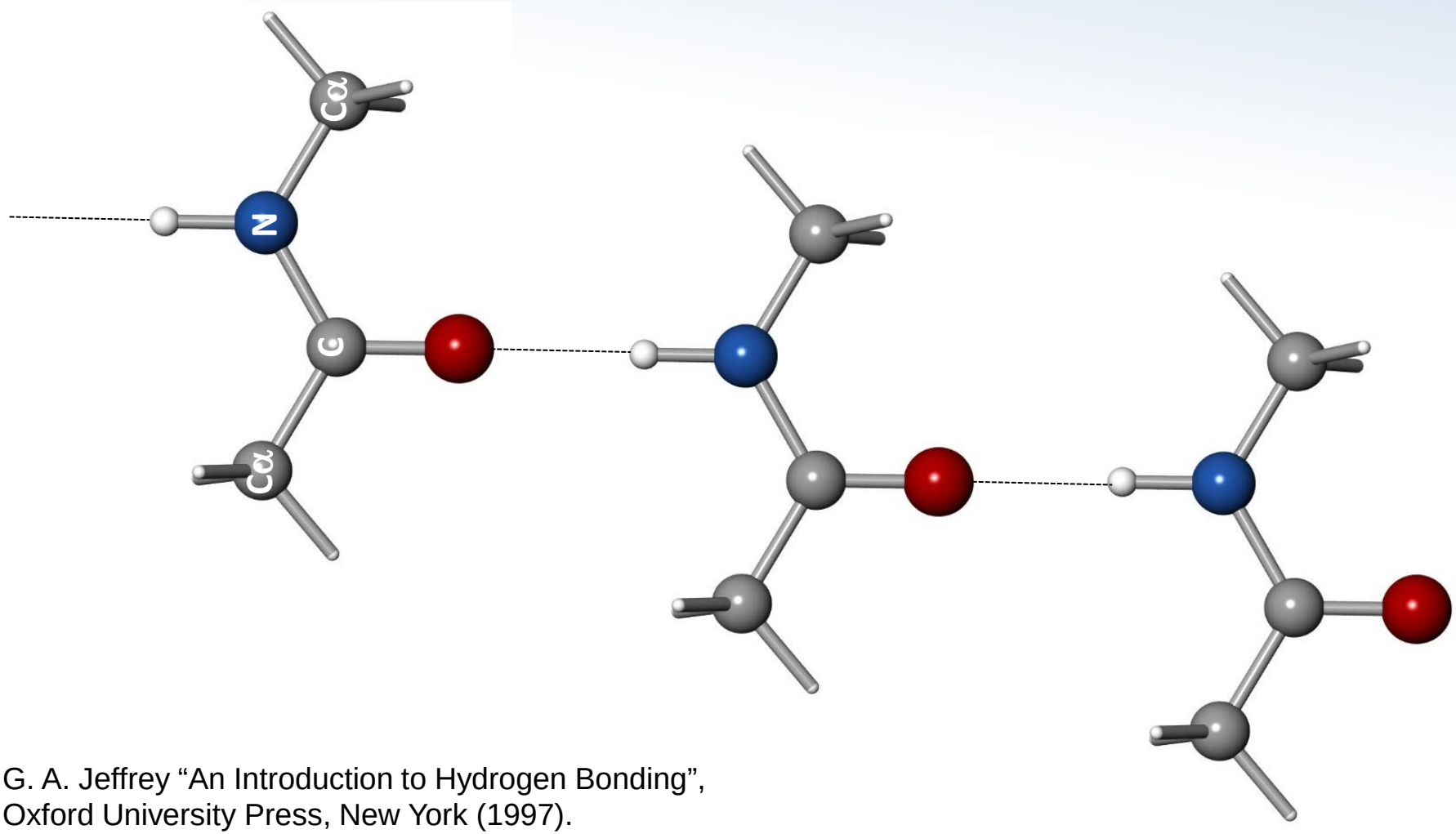
Introduction

In proteins water may mediate in C=O···H-N to nucleate protein folding or in the protein surface where they are exposed to hydrophilic interactions



Introduction

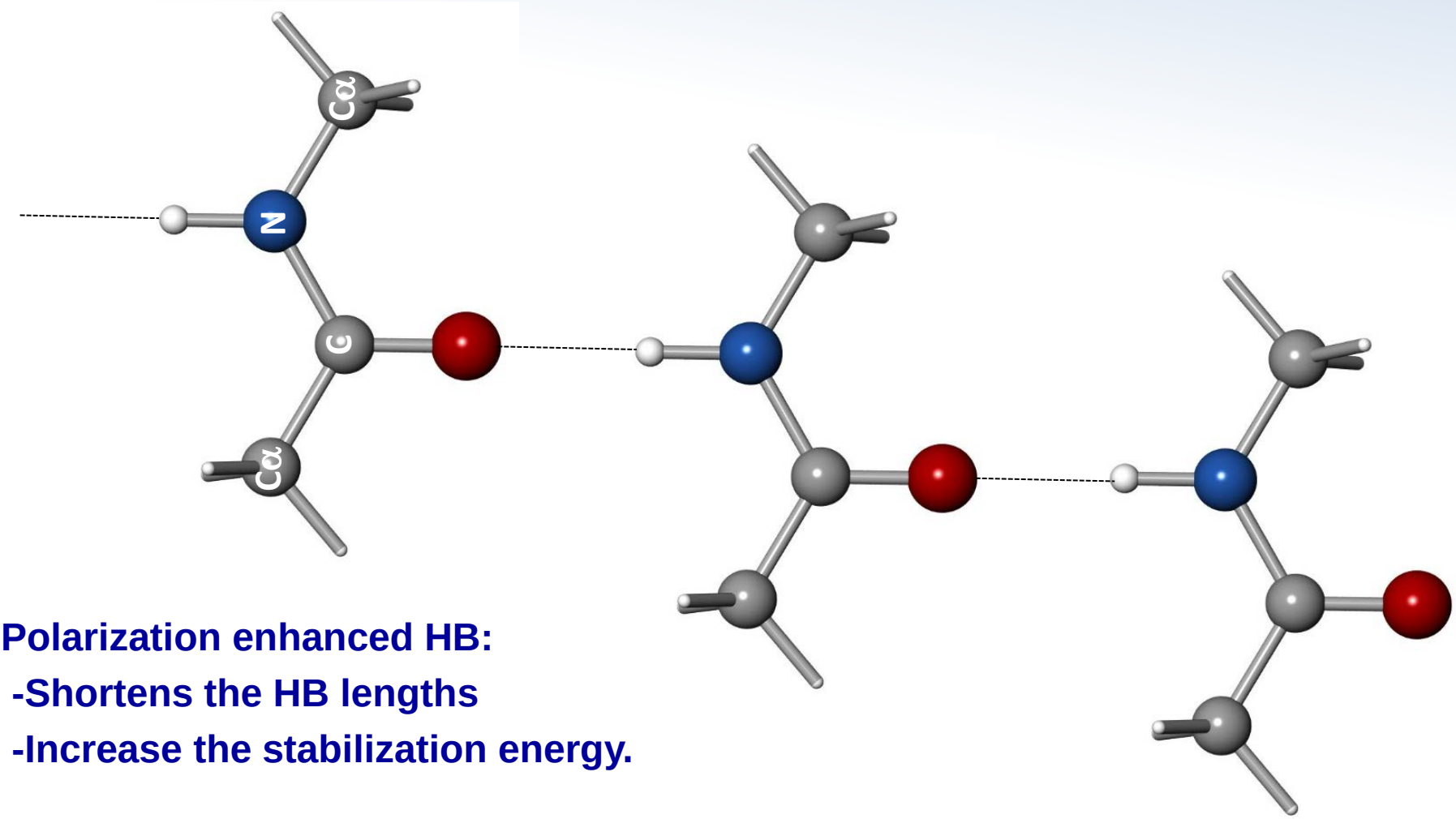
Cooperative effects may play an important stabilization role:



G. A. Jeffrey “An Introduction to Hydrogen Bonding”,
Oxford University Press, New York (1997).

Introduction

Cooperative effects may play an important stabilization role:



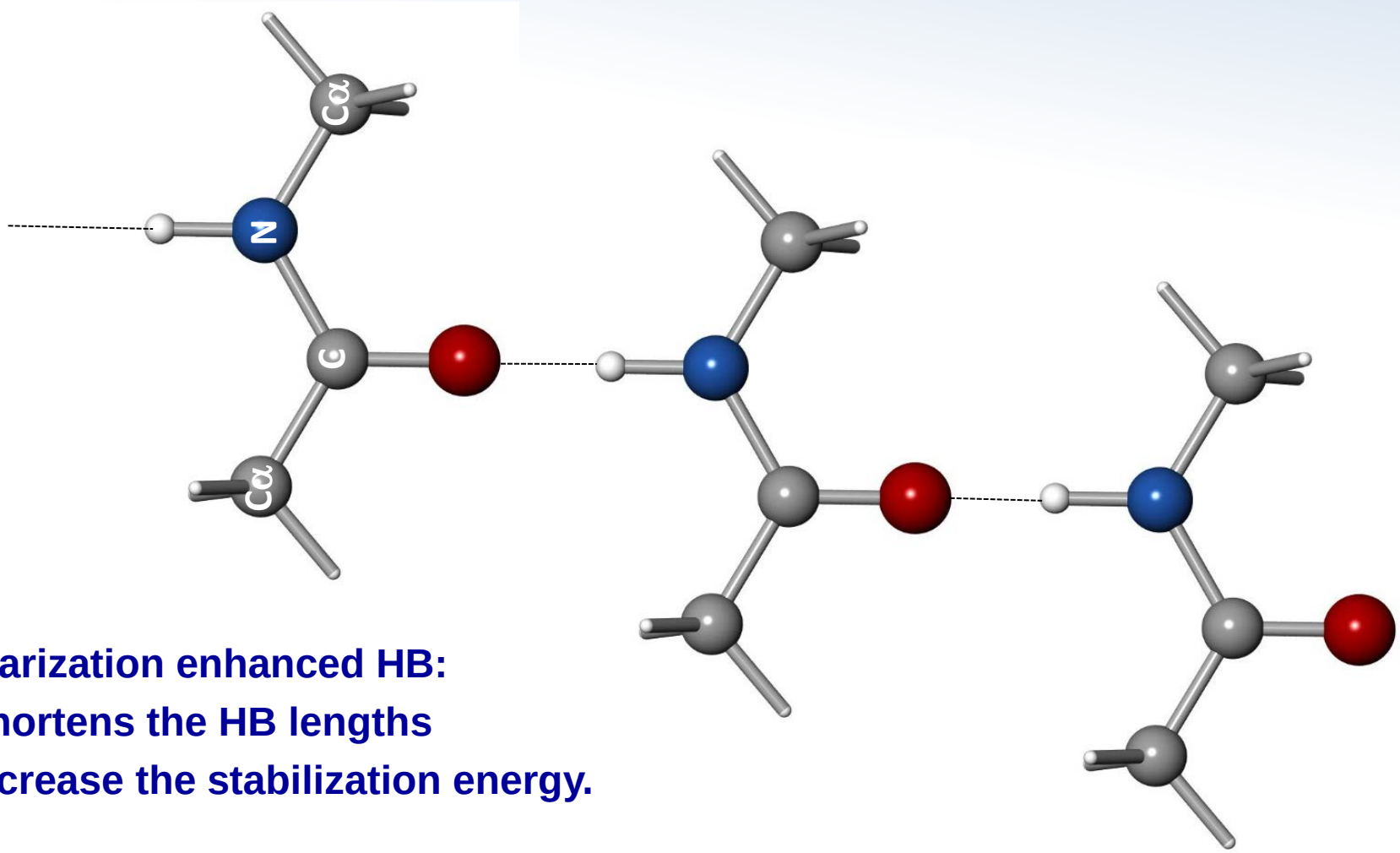
Polarization enhanced HB:

-Shortens the HB lengths

-Increase the stabilization energy.

Introduction

Cooperative effects may play an important stabilization role:



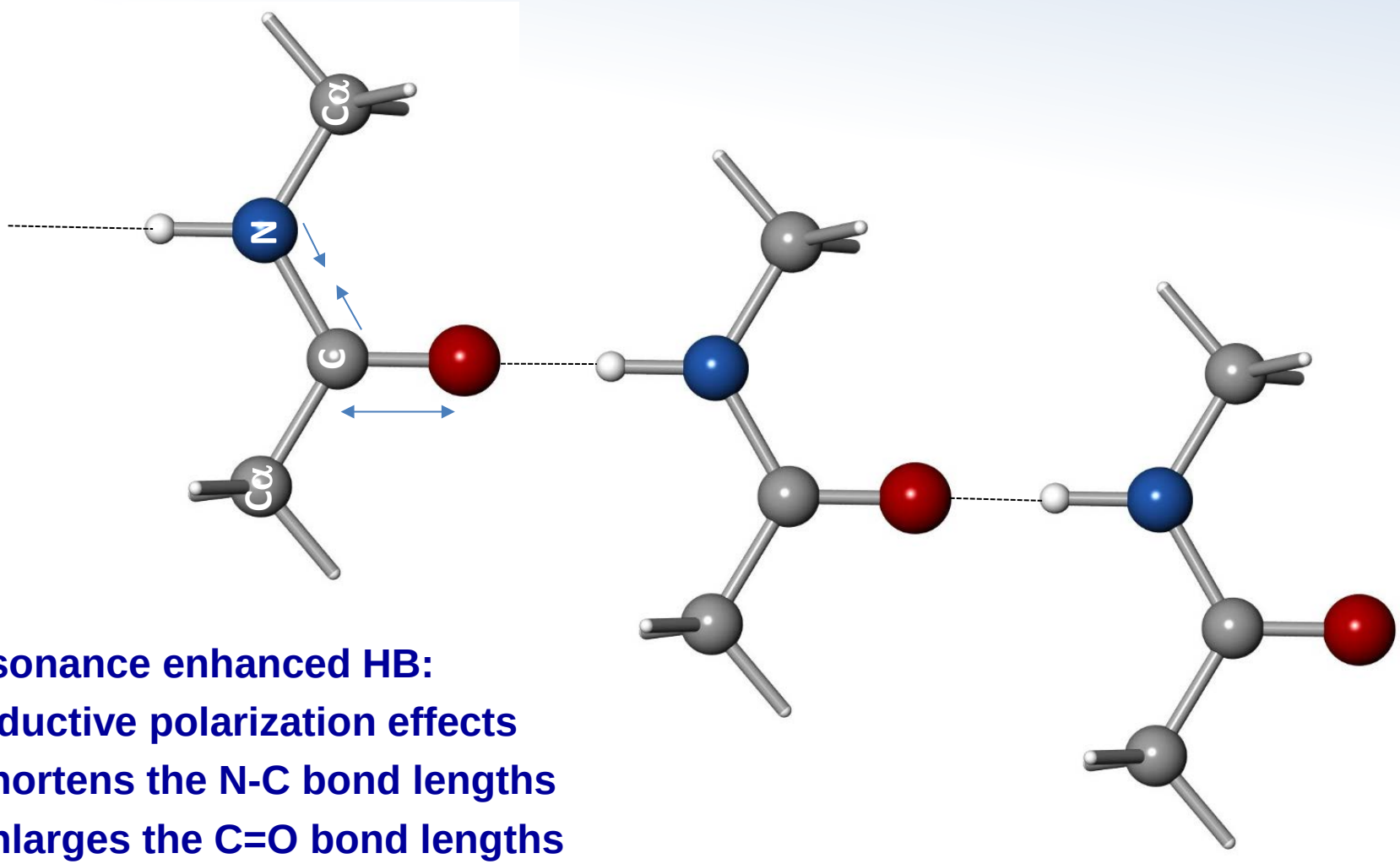
Polarization enhanced HB:

-Shortens the HB lengths

-Increase the stabilization energy.

Introduction

Cooperative effects may play an important stabilization role:



Resonance enhanced HB:

-Inductive polarization effects

-Shortens the N-C bond lengths

-Enlarges the C=O bond lengths

Previous studies

The interactions with water have be modelled from the study of gas phase **microsolvated** clusters of simple molecules having the peptide group:

Some examples from MW spectroscopy

formamide-$(H_2O)_n$, n=1,2 : F. J. Lovas et al. *J. Chem. Phys.* **1988**, *88*, 722; S. Blanco *et al*., JACS, *J. Am. Chem. Soc.* **2006**, *128*, 12111.

N-methylformamide-(H_2O): W. Caminati, *et al*., *Phys. Chem. Chem. Phys.* **2010**, *12*, 10230–10234.

2-hydroxypyridine/2-pyridone-formamide-$(H_2O)_n$, n=1,2: A. Maris et al, Chem. Phys. Lett. 2002, 360, 155; S. Mata, *et al*. J. Phys. Chem. A 2010, 114, 11393–11398.

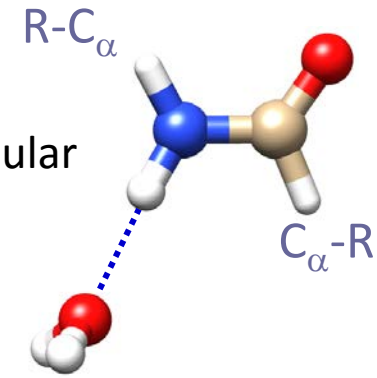
2-azetidinone-$(H_2O)_n$, n=1,2: J. C. López et al., PCCP, 2015, 17, 2054.

alaninamide-(H_2O): R. J. Lavrich, M. J. Tubergen, J. Am. Chem. Soc. 2000, 122, 2938–2943.

Formamide-water complexes

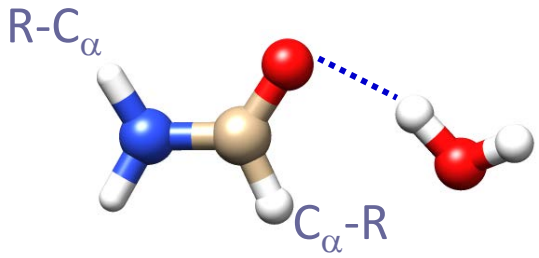
The observed **1:1** clusters of **formamide** with **water** cover all possible hydrogen bond situations:

trans-peptide



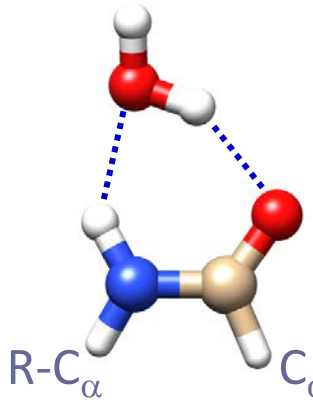
FW-1:1c

14% In globular proteins



FW-1:1b

cis-peptide



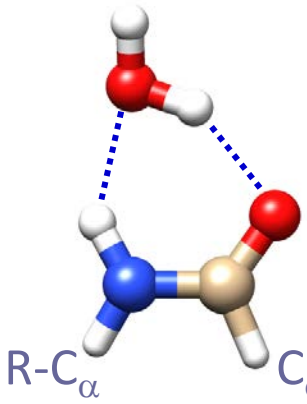
FW-1:1a

42% in globular proteins

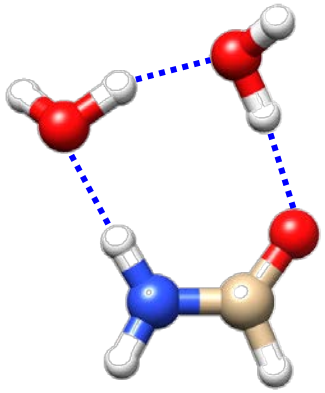
S. Blanco *et al*., JACS, *J. Am. Chem. Soc.* **2006**, *128*, 12111

Formamide-water complexes

The signatures of polarization enhanced HB have observed when the structures of sequential 1:1 and 1:2 cycles:



FW-1:1a



FW-1:2a

Shortening of HB lengths

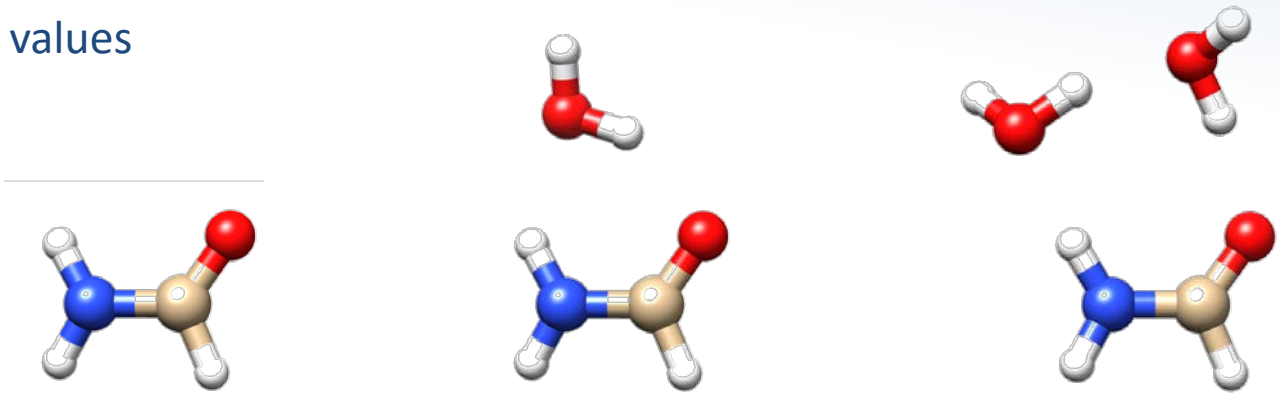
Stabilization energy

S. Blanco *et al*., JACS, *J. Am. Chem. Soc.* **2006**, *128*, 12111

Formamide-water complexes

However no experimental evidence of changes in the r(C-N) or r(C=O) bond lenghts.

Ab initio values



r_{C-N} = 1.361 Å
$r_{C=O}$ = 1.219 Å

1.350 Å
1.226 Å

1.343 Å
1.229 Å

r(C-N) decrease

r(C=O) increase

S. Blanco *et al.*, JACS, *J. Am. Chem. Soc.* **2006**, *128*, 12111

Formamide-water complexes

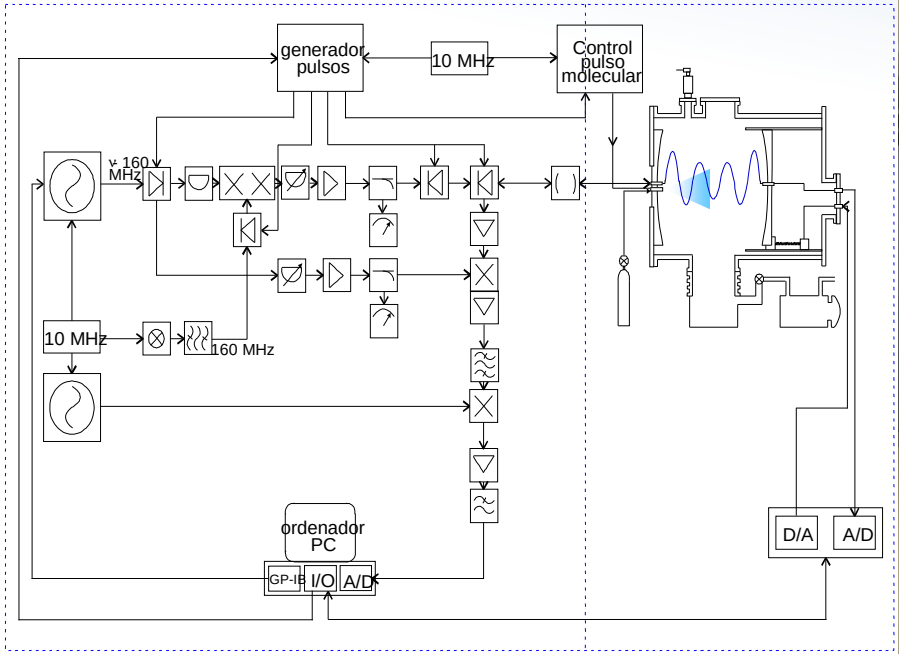
We have extended the study of formamide water clusters to new species: $(formamide)_2$-H_2O[1] and formamide-$(H_2O)_3$

To characterize their structure and dynamics

To find the signatures of cooperative effects.

Experiment

Spectrum



FTMW spectrometer

MB-FTMW (4-16 GHz)

Chem. Phys. 218 267 (1997); Chem. Phys. 119 880 (2003)

Summary

- Formamide$_2$-water (f_2w) can be taken as a microsolvated water cluster being formamide the solvent and as a model for water mediated amide interactions and self-association.

- Unambiguous structure characterization based on the observation of isotopologues and hyperfine structure analysis

- The structure of f_2w show for the first time in gas phase the effect of resonance enhanced cooperative hydrogen bonding of an amide

- Quadrupole coupling constants are a precious tool to detect the existence on inductive effects due to cooperativity polarization.

Acknowledgement

- **Thank you for your attention!**